

PATENT COOPERATION TREATY

PCT

**NOTIFICATION OF THE RECORDING
OF A CHANGE**

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SWANSON, Barry, J.
Swanson & Bratschun, L.L.C.
Suite 330
1745 Shea Center Drive
Highlands Ranch, CO 80129
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 25 January 2002 (25.01.02)	
Applicant's or agent's file reference NEX 85/PCT	IMPORTANT NOTIFICATION
International application No. PCT/US00/20625	International filing date (day/month/year) 28 July 2000 (28.07.00)

1. The following indications appeared on record concerning: <input checked="" type="checkbox"/> the applicant <input type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative		
Name and Address NEXSTAR PHARMACEUTICALS, INC. Suite 200 2860 Wilderness Place Boulder, CO 80301 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: <input checked="" type="checkbox"/> the person <input checked="" type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence		
Name and Address GILEAD SCIENCES, INC. 333 Lakeside Drive Foster City, California 94404 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to: <div style="display: flex; justify-content: space-between;"> <div> <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the International Searching Authority <input checked="" type="checkbox"/> the International Preliminary Examining Authority </div> <div> <input type="checkbox"/> the designated Offices concerned <input checked="" type="checkbox"/> the elected Offices concerned <input type="checkbox"/> other: </div> </div>		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Carlos NARANJO Telephone No.: (41-22) 338.83.38
--	---

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: BARRY J. SWANSON
SWANSON & BRATSCHEUN, L.L.C.
1745 SHEAR CENTER DRIVE
SUITE 330
HIGHLANDS RANCH CO 80129

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing
(day/month/year)

18 JAN 2002

Applicant's or agent's file reference
NEX 85/PCT

IMPORTANT NOTIFICATION

International application No.

PCT/US00/20625

International filing date (day/month/year)

28 JULY 2000

Priority Date (day/month/year)

29 JULY 1999

Applicant

NEXSTAR PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Authorized officer

KAREN A. LACOURCIERE

JOYCE BRIDGERS

PARALEGAL SPECIALIST
CHEMICAL MATRIX

Facsimile No. (703) 305-3230

Telephone No. (703) 305-1235

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NEX 85/PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/20625	International filing date (day/month/year) 28 JULY 2000	Priority date (day/month/year) 29 JULY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/04, 21/02; A61K 48/00 and US Cl.: 435/6, 91.1, 91.2; 935/77, 78; 514/44		
Applicant NEXSTAR PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 01 FEBRUARY 2001	Date of completion of this report 10 JANUARY 2002
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JOYCE BRIDGERS PARALEGAL SPECIALIST KAREN A. LACOURCIERE CHEMICAL MATRIX Telephone No. (703) 308-1235

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed☒ the description:

pages 1-22

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of

☒ the claims:

pages 23-25

, as originally filed

pages NONE

, as amended (together with any statement) under Article 19

pages NONE

, filed with the demand

pages NONE

, filed with the letter of

☒ the drawings:

pages 1-3

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of

☒ the sequence listing part of the description:

pages NONE

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig. NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 2

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 2.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☒ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/20625

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims	<u>1, 3-21</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>16-21</u>	YES
	Claims	<u>1, 3-15</u>	NO
Industrial Applicability (IA)	Claims	<u>1, 3-21</u>	YES
	Claims	<u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1 and 3-15 lack an inventive step under PCT Article 33(3) as being obvious over Gold et al. or WO 91/19813 in view of WO 98/30240.

Claims 1 and 3-15 are drawn to nucleic acid ligands to CD40 ligand and methods to isolate said nucleic acid ligands.

Gold et al. and WO 91/19813 each teach a general method of identifying nucleic acid ligands of a target protein throughout their disclosure wherein the methods comprise the same method steps as claimed in the instant application. Neither Gold et al. nor WO 91/19813 teach nucleic acid ligands to CD40 ligand nor do they teach using their methods to isolate ligands to CD40 ligand. WO 98/30240 teaches compounds which bind to and inhibit CD40ligand-CD40 binding interactions by binding to CD40ligand.

It would have been obvious at the time the instant invention was made to identify nucleic acid ligands to CD40ligand using the methods taught by Gold et al. or WO 91/19813 because Gold et al. and WO 91/19813 teach their methods as generally applicable to make a nucleic acid ligand for any desired target, even for proteins which do not normally bind nucleic acids (like CD40 ligand). One would have been motivated to isolate nucleic acid ligands to CD40 ligand because the interaction of CD40ligand with CD40 has an important role in the immune response and WO 98/30240 teaches that it is beneficial to identify compounds which bind to CD40ligand and interrupt its interaction with CD40. One would have expected to find nucleic acid ligands with this characteristic and would have expected to be able to practice these methods based on the disclosure of Gold et al. and WO 91/19813.

Claims 16-21 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest methods of treatment and pharmaceutical compositions using nucleic acid ligands which bind to CD40ligand.

____ NEW CITATIONS _____
NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference NEX 85/PCT	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/20625	International filing date (day/month/year) 28 JULY 2000	(Earliest) Priority Date (day/month/year) 29 JULY 1999
Applicant NEXSTAR PHARMACEUTICALS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: BARRY J. SWANSON
SWANSON & BRATSCHEUN, L.L.C.
1745 SHEAR CENTER DRIVE
SUITE 330
HIGHLANDS RANCH CO 80129

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference NEX 85/PCT	Date of Mailing <i>(day/month/year)</i> 30 NOV 2000
International application No. PCT/US00/20625	International filing date <i>(day/month/year)</i> 28 JULY 2000
Applicant NEXSTAR PHARMACEUTICALS, INC.	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer KAREN A. LACOURCIERE <i>Derry J. Dyfor</i> Telephone No. (703) 308-1235
---	--

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 2
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claim 2 is drawn to nucleic acid compounds which have a specific sequence, but a nucleotide sequence was not provided.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/20625

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04, 21/02; A61K 48/00

US-CL : 435/6, 91.1, 91.2; 935/77, 78; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.1, 91.2; 935/77, 78; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

BIOSIS, MEDLINE, CAPLUS, LIFESCI, EMBASE, USPATFULL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,270,163 A (GOLD ET AL.) 14 December 1993 (14.12.93), see entire document.	1, 3-21
Y	WO 98/30240 A1 (BIOGEN, INC.) 16 July 1998 (16.07.98), see entire document.	1, 3-21
Y	WO 91/19813 A1 (THE UNIVERSITY OF COLORADO FOUNDATION, INC.) 26 December 1991 (26.12.91), see entire document.	1, 3-21

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

08 NOVEMBER 2000

Date of mailing of the international search report

30 NOV 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

KAREN A. LACOURCIERE

Telephone No. (703) 308-1235